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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,353	04/11/2002	Edward S. Yeung	215390	6921
23460	7590	06/15/2004	EXAMINER	
LEYDIG VOIT & MAYER, LTD TWO PRUDENTIAL PLAZA, SUITE 4900 180 NORTH STETSON AVENUE CHICAGO, IL 60601-6780			STOCK JR, GORDON J	
			ART UNIT	PAPER NUMBER
			2877	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/031,353

Applicant(s)

YEUNG ET AL.

Examiner

Gordon J Stock

Art Unit

2877

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 April 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 and 57-91 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 and 57-91 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. **Claims 1, 3-8, 11-13, 15-18, 21, 22, 58, 60-62, 65, 67-72, 74-76, 78-80, 83, 84, 86, 88 and 89** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in view of **Craighead et al. (6,438,279)**.

As to **claims 1, 3-8, 11-13, 15-18, 21, 22, 58, 60-62** Simpson discloses the following: subjecting a sample comprising multiple molecules, at least one molecule is labeled to electrophoresis; imaging the mobility of each labeled molecule over time by detecting the position of the label over time; dispersing the imaging by a transmission grating; determining the electrophoretic mobility and the molecular spectrum; distinguishing molecules; at least one molecule is a nucleic acid and/or protein detectably labeled with a fluorescent dye; at least one small molecule may be a Sanger sequencing reaction fragment; said sample comprises a buffer; the at least one molecule with label has fluorescence induced by a laser; the fluorescence is focused on the imaging means; using an intensified CCD camera, TE/CCD 1023E detector from Princeton Instruments Inc.; laser filters are positioned in front of said imaging means; multiframe method is used; the mobility is imaged in less than about 5 milliseconds, 4000 frames per .1 second; at least one molecule is at a concentration of at least about 1 copy per milliliter, .5 microliters of sample was analyzed was loaded into the gel. The system comprising: an electrophoretic sample channel; a monochromatic light source that irradiates sample; imaging means; a transmission grating; a lens between said light source and sample for focusing light;

Art Unit: 2877

imaging means is an intensified CCD camera, TE/CCD 1023E detector; at least one filter, a laser filter; imaging means images 4000 frames per .1 second (Figs. 1, 2a, 2b, 3, 11-13, 14a, 14b, 17(1), 17(2), 18a, 18b; col. 5, lines 20-30 and 50-67; col. 6, lines 1-15 and 45-55; col. 7, lines 5-20 and 60-67; col. 8, lines 1-30; col. 9, lines 60-65; col. 10, lines 20-65; cols. 11-12; cols. 31-32; col. 40, lines 15-55).

As for at least one molecule individually being distinguished, Simpson suggests this with one strand of DNA being observed at one time (col. 42, lines 21-45). And teaches that the migration lanes are 25 microns or less in diameter (col. 5, lines 20-25). Craighead in a unitary microcapillary teaches using capillaries below 1 micron in order to distinguish individual molecules (col. 2, lines 1-35). Therefore, it would be obvious to one skilled in the art that the system can distinguish at least one molecule individually for the lanes may be 25 microns or less such as below 1 micron.

As to **claims 65, 67-72, 74-76, 78-80, 83, 84, 86, 88 and 89**, Simpson discloses the following: introducing a sample comprising multiple molecules in free solution at least one is detectably labeled into a sample channel; imaging the position of labeled molecule and dispersing image by a transmission grating; determining molecular spectrum; distinguishing at least one molecule; the molecule may be a labeled nucleic acid or protein; at least one small molecule may be a Sanger sequencing reaction fragment; sample comprises a buffer; the labeled sample is fluoresced by a laser; there is focusing of the fluorescent label on imaging means; an intensified CCD camera, TE/CCD 1023E detector, comprises the imaging means; a laser filter is positioned before the imaging means; imaging happens in 4000 frames per .1 second; .5 microliters of sample is analyze. The system itself comprises the following: a sample channel; a

Art Unit: 2877

light source of one wavelength that irradiates labeled molecules; imaging means; transmission grating; a lens between light source and channel for focusing; a TE/CCD 1023E detector; a laser filter; imaging means images 4000 frames per .1 second. (Figs. 1, 2a, 2b, 3, 11-13, 14a, 14b, 17(1), 17(2), 18a, 18b; col. 5, lines 20-30 and 50-67; col. 6, lines 1-15 and 45-55; col. 7, lines 5-20 and 60-67; col. 8, lines 1-30; col. 9, lines 60-65; col.10, lines 20-65; cols. 11-12; cols. 31-32; col. 40, lines 15-55).

As for at least one molecule individually being distinguished, Simpson suggests this with one strand of DNA being observed at one time (col. 42, lines 21-45). And teaches that the migration lanes are 25 microns or less in diameter (col. 5, lines 20-25). Craighead in a unitary microcapillary teaches using capillaries below 1 micron in order to distinguish individual molecules (col. 2, lines 1-35). Therefore, it would be obvious to one skilled in the art that the system can distinguish at least one molecule individually for the lanes may be 25 microns or less such as below 1 micron.

3. **Claims 2 and 66** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in view of **Craighead et al. (6,438,279)** further in view of **Fan (60/180810)**.

As for **claims 2 and 66**, Simpson in view of Craighead discloses everything as above (see **claims 1 and 65 above**). Simpson is silent concerning not amplifying multiple molecules prior to electrophoresis. However, Fan in a gene expression profiling method teaches profiling molecules without target-specific amplification (introduction; Parts I-III of pages 5-8). Therefore, it would be obvious to one skilled in the art to have the method comprise removing

Art Unit: 2877

amplification in order to provide a more accurate and sensitive approach to profiling and to remove the excess steps due to amplification to save time in molecule monitoring.

4. **Claims 9, 10, 73**, are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in view of **Craighead et al. (6,438,279)** further in view of **Schwartz et al. (6,221,592)** and **Chu (5,215,883)**.

As to **claims 9, 10, 73**, Simpson in view of Craighead discloses everything as above (see **claims 8 and 72**). Simpson is silent concerning photobleaching. However, Schwartz in nucleic acid sequencing teaches photobleaching for eliminating fluorescence signals between cycles and to eliminate bulky moieties after they have served their purpose (col. 33, lines 55-67). In addition, Chu in electrophoretic system teaches photobleaching for demarcation of areas for detection (col. 8, lines 10-50). Therefore, it would be obvious to one skilled in the art to photobleach the buffer in order to eliminate possible fluorescent signals after certain substituents have served their purpose and/or possibly to demarcate areas for detection. Simpson does disclose a sieving matrix (col. 19, lines 60-67).

5. **Claims 14, 23, 57, 77, 85** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in view of **Craighead et al. (6,438,279)** further in view of **Yguerabide et al. (6,586,193)** and **Hayashizaki et al. (6,120,667)**.

As to **claims 14, 23, 57, 77, 85**, Simpson in view of Craighead discloses everything as above (see **claims 12, 21, 22, 75, 84** above). Simpson is silent concerning a pinhole and equilateral prism. Yguerabide teaches in an analyte assay using labels that equilateral prisms are used to enhance to signal to noise (col. 59, lines 20-45). Therefore, it would be obvious to one skilled in the art to have the system comprise an equilateral prism to enhance signal to noise of

Art Unit: 2877

the system. Hayashizaki in an electrophoresis apparatus teaches a pinhole to limit the detection field (col. 7, lines 15-25). Therefore, it would be obvious to one skilled in the art to have the system comprise a pinhole in order to limit the detection field.

6. **Claims 19, 20, 63, 64, 81, 82, 90, 91** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in view of **Craighead et al. (6,438,279)**.

As to **claims 19, 20, 63, 64, 81, 82, 90, and 91**, see **claims 1, 21, 65, and 83** above. As for the acquisition rates Simpson is silent. However, the acquisition rate depends on several factors such as electrode voltage, electrophoretic mobility, frame rate, image processing rate, and fluorescence. This acquisition rate would be considered an optimized value. Simpson discloses the claimed invention except for the particular acquisition rates. It would have been obvious to one having ordinary skill in the art at the time of the invention was made to have the particular acquisition rates, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980)

7. **Claims 59 and 87** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in view of **Craighead et al. (6,438,279)** further in evidence of **Brumley et al. (5,538,613)**.

As for **claims 59 and 87**, Simpson discloses everything as above (see **claims 58 and 86**). In addition, Simpson discloses objective lenses (col. 12, lines 1-40). In addition, Brumley in an electrophoresis analyzer teaches using a microscope objective for focusing (Fig. 1). Therefore, it would be obvious to one skilled in the art at the time the invention was made to have the system comprise a microscope objective lens to focus light to the imaging means.

Art Unit: 2877

Response to Arguments

8. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection. As for the rejections of claims 7 and 71 under 35 U.S.C. 112 second paragraph, the Examiner finds applicant's arguments from April 5, 2004 persuasive. Subsequently, the rejection of claims 7 and 71 under 35 U.S.C. 112 second paragraph has been withdrawn.

Fax/Telephone Numbers

If the applicant wishes to send a fax dealing with either a proposed amendment or a discussion with a phone interview, then the fax should:

- 1) Contain either a statement "DRAFT" or "PROPOSED AMENDMENT" on the fax cover sheet; and
- 2) Should be unsigned by the attorney or agent.

This will ensure that it will not be entered into the case and will be forwarded to the examiner as quickly as possible.

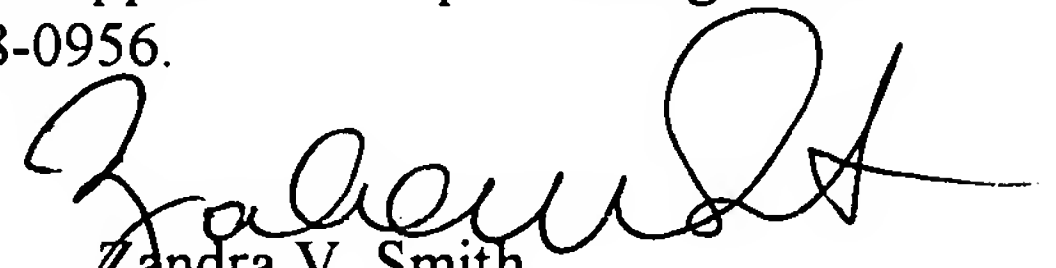
Papers related to the application may be submitted to Group 2800 by Fax transmission. Papers should be faxed to Group 2800 via the PTO Fax machine located in Crystal Plaza 4. The form of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CP4 Fax Machine number is: (703) 872-9306

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gordon J. Stock whose telephone number is (571) 272-2431. The examiner can normally be reached on Monday-Friday, 10:00 a.m. - 6:30 p.m.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0956.


gs

June 7, 2004


Zandra V. Smith
Primary Examiner
Art Unit 2877